Field: **Title**, Limits: **Publication Date from 1980 to 2001**

1: Nat Med. 1996 May;2(5):545-50.

Immune responses to transgene-encoded proteins limit the stability of gene expression after injection of replication-defective adenovirus vectors.

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The use of replication-defective adenoviruses (RDAd) for human gene therapy has been limited by host immune responses that result in transient recombinant gene expression in vivo. It remained unclear whether these immune responses were directed predominantly against viral proteins or, alternatively, against foreign transgene-encoded proteins. In this report, we have compared the stability of recombinant gene expression in adult immunocompetent mice following intramuscular (i.m.) injection with identical RDAd encoding self (murine) or foreign (human) erythropoietin. Our results demonstrate that immune responses direct against foreign transgene-encoded proteins are the major determinants of the stability of gene expression following i.m. injection of RDAd. Moreover, we demonstrate long-term recombinant gene expression in immunocompetent animals following a single i.m. injection of RDAd encoding a self protein. These findings are important for the design of future preclinical and clinical gene therapy trials.

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Gene therapy and viral vaccination: the interface.
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Live viral vaccines have had a major impact on the incidence of acute virus infections world-wide. Virus infections recognised as future vaccine targets will require a modified approach based on a detailed understanding of the immunobiology of specific infections combined with the application of new technologies designed to generate specific and appropriate protective immunity. A similar vector technology directed at in vivo gene delivery is currently being exploited both for gene therapy and vaccination. The induction of an immune response to an expressed transgene represents a potential hazard for a gene therapy protocol but is the object of a vaccine strategy. In vivo gene delivery using replication-competent or replication-deficient viral vector systems and by direct transfer of naked DNA can generate an effective humoral, secretory and cell-mediated immune response to expressed transgenes.